Remarks

Claims 1-3 and 9 and 17 are pending. Claims 1 has been amended. Claims 4-8 and 11-16 have been canceled. Claim 17 has been added. Support for the claim amendments and new claim can be found throughout the specification, and specifically in the sections discussing the wild type and various mutants of vaccinia virus. For example, Figure 2 shows that wild type vaccinia virus grow in both cancerous and non-cancerous cells, Figures 4, 7 and 11 show that E3LΔ54N is selective for cancerous cells, and Figure 9 shows that E3LΔ83N shows morbidity in mice.

Priority

The Office Action indicates that if the Applicants desire to claim the benefit of a prior-filed application under 35 U.S.C. § 120, a specific reference to the prior-filed application in compliance with 37 CFR § 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. The specification has been amended to claim priority to the U.S. Provisional application and the PCT application. Thus, Applicants respectfully request withdrawal of this objection.

Specification

The Office Action objects to the specification, indicating that the abstract does not commence on a separate sheet in accordance with 37 CFR § 1.52(b)(4). The specification is amended herein to provide a new abstract page on a separate sheet in accordance with 37 CFR 1.72.

Rejection Under 35 U.S.C. § 102

Claims 1 and 3-10 were rejected under 35 U.S.C. § 102(e) as being anticipated by Roberts et al. (2003/00444384). In addition, claims 1 and 4-8 were rejected under 35 U.S.C. § 102(b) as being anticipated by Lee et al. (Virology 1994, 199:491-496). Applicants respectfully traverse these rejections to the extent that they are applied to the claims as amended.

While the Examiner argues that Roberts et al. suggests a modified vaccinia virus having mutant E3L gene for the purpose of making the vaccinia virus resistant to interferon, Roberts et al. do not provide any guidance as to which mutations would result in this phenotype while

maintaining viral replication, and therefore oncolytic activity. As shown in Figure 4 of the present application, a full deletion of E3L results in the failure of the vaccinia virus to replicate in either normal or cancerous breast cells, and is therefore not oncolytic. In contrast, Figure 2 shows that wild type vaccinia virus are capable of replicating in both normal and cancerous cells and are therefore not selective for cancerous cells. Thus, something less than a full deletion of E3L is required for the mutant vaccinia virus to replicate and to be oncolytic while deletion of some part of E3L is required for selectivity. The present application shows that treatment of breast cancer xenografts with E3LΔ83N mutant vaccinia virus resulted in toxicity and morbidity. Thus, a deletion of less than the amino-terminal 83 amino acids is necessary for the vaccinia virus to be efficacious *in vivo*. As demonstrated in the description of Figure 11, vaccinia virus having the E3LΔ54N truncation selectively and effectively induced oncolytic regression of breast cancer xenografts. Thus, if a vaccine virus is used having a truncation, particularly a truncation at the amino terminus of E3L which is less than 83 amino acids, and which can replicate in human breast cancer cells but not in normal breast cells, this vaccinia virus can be used to induce lysis of proliferating cancer cells.

As can be seen in Figure 1, mutations having a truncation at the amino terminus or the carboxy terminus but having a truncation of less than 83 amino acids at the amino terminus have the optimal combination of PKR inhibition and high ras dependency. The mutants as now claimed, wherein the E3L gene is truncated, do not replicate in normal breast cells, which is critical for oncolytic activity. The specification provides a test to assess whether a mutant selectively replicates in breast cancer cells but not normal cells. This test is outlined in paragraphs [0035], [0037] and [0040]. Viral replication is determined by measuring how many infectious viral particles are present after 72 hour of culturing (*see* paras. [0035], [0037]), and by measuring viral protein synthesis after 72 hours (*see* para. [0040]). Thus, the present specification has described and enabled the claimed vaccinia virus mutants and provides guidance for selecting truncations of less than 83 amino-terminal residues, such as about 54 residues.

Thus, in order to facilitate prosecution, Applicants have amended claim 1 to recite "a vaccinia virus having a truncation mutation in E3L of less than 83 amino acids from the amino terminus, wherein the vaccinia virus selectively replicates in cancer cells" and canceled claims 4-

8. In addition, claim 17 has been added, reciting "wherein the vaccinia virus has a truncation mutation in E3L of about 54 amino acids from the amino terminus." Support for these amendments can be found in the description of Figure 11 in the specification, showing the oncolytic regression of breast cancer xenografts using vaccinia virus having the E3LΔ54N truncation versus the toxicity and morbidity associated with mutant vaccinia virus having the E3LΔ83N truncation.

As neither Roberts et al. nor Lee et al. specifically teach or suggest the partial truncations of E3L disclosed in the instant application or its equivalents, the rejection is rendered moot. Applicants, therefore, respectfully request the withdrawal of this rejection and allowance of claims 1-3 and 9-10.

Rejection Under 35 U.S.C. § 103

Claims 1 and 2 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Roberts et al, in view of Coffey et al. (2002/0028195). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended. As discussed above, Roberts et al. do not teach or suggest the E3LΔ83N or E3LΔ54N partial truncations disclosed in the instant application or their equivalents, and Coffey et al. do not cure the deficiencies of Roberts et al. Applicants, therefore, respectfully request the withdrawal of this ground of rejection.

CONCLUSION

If a telephone interview would be of assistance in expediting prosecution of the subject application, Applicants invite the Examiner to telephone the undersigned at the number provided below.

The Commissioner is hereby authorized to charge any fees required or credit any overpayment for this filing to Womble Carlyle Sandridge & Rice, PPLC Deposit Account No. 09-0528.

Respectfully submitted,
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Date: February 8, 2008

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